

BLOOD EXAMINATIONS IN THE SURGERY OF THE NOSE AND THROAT.

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The more than occasional reference in the literature of cases of severe or even fatal hemorrhage following operations upon the nose and throat and particularly operations for the removal of the lymphoid tissue of the nasopharynx and faucial tonsils and the undoubted existence of a goodly number of fatalities which are unpublished and hidden away in the memories of the operator, leads to much thought as to why these procedures should be fraught with so many more complications of this nature than in other general surgical interventions. Is it due to a lack of pre-operative understanding of the individual, or to unusual abnormalities found with greater frequency in these regions?

Harmon Smith reports in an article many years ago, a series of over fifty cases compiled from the literature, of alarming hemorrhage after tonsilotomy. I must, however, take exception to his statement as to the careful attention drawn to this subject in the textbooks. I have been unable to find anything more than the crudest casual reference in the works I have consulted.

May I be so bold as to say that it is a lamentable fact that of all those in the medical profession who would dare do any kind of a surgical operation, probably more have had the temerity to attempt operations on the nose and throat with less knowledge of their anatomy, than upon any other part of the human body.

I find constant explanation being mentioned in published cases of abnormal position of blood vessels and other lame excuses, for upon a critical analysis of the case, in most instances, the resultant complication has been due to a lack of sufficient preliminary investigation of the patient to be operated or, in some cases, a very decided error in technique. The haphazard calling of a case a bleeder, as an explanation without warrantable facts, is as poor a diagnostic excuse as hysteria, they both cover a multitude of sins and have eased the conscience of a multitude of occasional surgeons and shielded the inability or futile efforts of the more experienced.

There is an old adage, "He who lives in a glass house must pull down the blinds," and I myself must plead guilty in my earlier

experiences to the very things which I am making this plea to correct. I have but to cite the following instance:

An opera singer under my care had a lymphoid mass at the base of the tongue, which interfered with her high note vocalization. Her history was that five years previous, a very celebrated laryngologist had removed her tonsils, and for a period of nearly a week following, there was a constant succession of secondary hemorrhages, which finally ceased after a ligation of the carotid artery. This history I accepted with due consideration, but there had been nothing in my observation of this patient which led me to any conclusion but that the bleeding had been due to anything other than poor surgical technique. I accordingly guillotined a mass from the base of her tongue. Four hours later a secondary hemorrhage took place and I spent the remaining thirty hours in attendance upon her. Can you imagine a more difficult place to control a hemorrhage in the nature of a steady ooze? Had I the knowledge of the value of blood examinations at that time, I would have determined in advance of the operation that which I subsequently ascertained, that this patient was a true haemophilic.

It is not the purpose of this paper to take up the question of the type of operative procedure, but I must make reference to the universal diversity of the plan of attack. Each operator seems to have a particular pet method. For example: in recently observing six different men in the course of one afternoon operate at one of our prominent clinics, each operated by a different method, and while I grant that every road may lead to Rome, yet some have pitfalls and are headed straight for the cemetery.

Upon close inquiry, I found that of the large number of these cases, some twenty-six which I saw operated at that particular clinic, they had either entered the hospital the previous night, or the day of the operation and that only a local examination of these children's noses and throats had been made. I am satisfied that some of these cases had had a very recent acute infection of the upper respiratory tract and probably were still running temperature or having considerable bronchial cough or a nasal secretion suggestive of an ethmoidal infection.

In one, the character of the nasal discharge with the excoriated condition of the muco-cutaneous juncture of the nose would, to my mind, have suggested a possible nasal diphtheria. In not a single instance was a blood examination made to determine whether or no a haemophilic or purpuric tendency was present. Three of these

manifested a sufficiently troublesome amount of bleeding to have suggested very strongly to my mind that such a dyscrasia was underlying, although in one case I could not help but reflect that the use of the bistoury was rather an antiquated method of operation and one attendant with the possibilities of inviting disaster.

The invariable practice of controlling the bleeding was by compression. Only one operator of this group resorted to the use of the haemostatic forceps. Many of these cases left the operating table oozing and, I am satisfied, subsequently vomited up large quantities of swallowed blood. Observations of this kind raise the thought as to why should throat surgeons perform surgical procedures differently than the general surgeons? Would the abdominal surgeon rely upon compression and close the wound without securely ligating every bleeding surface? If not, why should throat surgery be performed along such indifferent and careless lines?

It is not, however, the object of these remarks to dwell upon this phase of the subject, but rather to take up some consideration of the subject of the blood under normal and hemorrhagic conditions and to make reference to the great importance and preoperative value of blood examinations preliminary to operative work upon these parts, for to be forewarned is to be forearmed, and the safeguarding of the patient is the safeguarding of our own reputation.

Under normal conditions, when blood escapes from the blood vessels either into the tissues or outside of the body, coagulation takes place in from three to ten minutes. If the blood were to be removed from one of the blood vessels without first coming into contact with the tissues it would require a longer time to become jellied throughout. The same blood that coagulates in between three and ten minutes, when removed directly from the blood vessels may require thirty to forty minutes for coagulation. Almost all of the methods suggested for the determination of coagulation time fail to recognize what physiologists demonstrated long ago, that contact with the tissues markedly accelerates the coagulation time of the blood.

After the coagulated blood has stood for a short time the fibrin in the clot contracts, holding in it the enmeshed blood cells, and a straw colored fluid is expressed, which is known as serum.

Numerous theories have been advanced concerning the reason for the coagulation of blood and the one of Howell is probably most generally accepted, because each step is supported by experimental evidence. We may briefly summarize as follows: the final product, fibrin, does not exist as such in the blood, but is formed from its

precursor, fibrinogen, by the action of thrombin upon it. Thrombin is a protein substance. It does not exist in the circulating blood, but is formed by the inter-reaction of prothrombin and calcium salts. The activation of prothrombin does not occur normally while the blood is still in the blood vessels; it occurs only after the bleeding has taken place, for the reason that in the blood there is a substance which prevents the formation of thrombin and has been called anti-thrombin. The blood platelets and blood cells, when they undergo disintegration, and the lacerated tissues produce a substance which neutralizes anti-thrombin and allows thrombin to be formed by the combination of calcium salts and prothrombin. "Thromboplastic substances" is the term given to those materials which nullify the action of anti-thrombin. Howell has isolated a phosphatid which he calls "kephalin," which substance has the power to counteract the action of anti-thrombin.

Many methods have been devised for the estimation of coagulation time. Some have involved the removing of blood from a vein; others with the obtaining of blood by puncturing the skin. The removal of blood directly from the vein necessarily must exclude the action of thromboplastic substances derived from lacerated tissues and the blood will not coagulate as quickly as the blood removed by puncturing the skin.

Of course, this method does not give us a fair index of the coagulability of the blood, comparable with that which obtains after an operation. After a surgical procedure, the blood exudes over cut or lacerated tissues and gains the action of the thromboplastic substances from the cut or lacerated tissues in addition to the substances produced by the disintegration of the blood platelets and blood cells. We have adopted a method which is most serviceable in relation to nose and throat surgery. The skin is punctured with a needle having a knife edge and the blood is sucked into a 0.2c.c. pipette, such as is used in serological work. The blood is then allowed to flow to about the center of the pipette and it is then placed in the thermostat at 37° C., and observed every two minutes. From time to time a small drop of blood is blown on to a glass slide to determine whether coagulation has started. When coagulation is complete, it is very difficult to blow the blood from the pipette. Very often the blood, after having coagulated, does not contract and does not attach itself to the sides of the pipette and flows readily upon holding the pipette in an upright position. For this reason, it is always necessary to blow a drop on to a glass slide to determine

the presence of a clot. By allowing the blood to flow to about the center of the pipette, we avoid as much as possible any action on the blood which may occur as the result of drying while in the thermostat. With this method the coagulation time was estimated in over 400 cases, the average time being 6.3 minutes; the most prolonged coagulation time was 29 minutes, and the shortest was $1\frac{1}{2}$ minutes.

In connection with this work, it is always necessary to determine the bleeding time for the reasons that will be mentioned later. The bleeding time is determined by noting the time when the skin is pierced and observing how long it will bleed by gently squeezing the part from time to time. The bleeding time was determined in nearly 200 of the cases above cited; the average time was 5 minutes, the longest bleeding time 29 minutes, and the shortest, 2 minutes. The coagulation time may be prolonged and the bleeding time may be short, or vice versa, or both may be prolonged.

Two conditions namely haemophilia and purpura, demand especial attention in connection with this work, for if they are not recognized before an operation is performed, they may give rise to complicating conditions which may even jeopardize the patient's life.

In no case where either the bleeding time or coagulation time varied much beyond the limits of normality, was operation undertaken without preliminary preparation to improve the altered blood condition. If this was not successfully accomplished, as occurred in a few instances, a refusal to operate was emphatically made. I have often wondered what occurred in one particular case where I had refused to operate, that had subsequently been operated by another physician, for in questioning him on the subject he has been singularly reticent. I do know, however, of some very uncharitable remarks made of him and which have reached my ears from lay sources.

Haemophilia is an hereditary disease transmitted through the female to the male offspring. It is characterized by greatly increased coagulation time, and as the result of an individual receiving a slight wound, it may prove the cause of his death. The true etiology of haemophilia is not yet known. It was presumed at one time that the delayed coagulation time was due to an increased amount of anti-thrombin, but subsequent investigation has proven the falsity of this supposition. It was then thought that there was in the blood of these patients a smaller quantity of calcium salts than normally exists. A series of several cases having a delayed coagulation time

were prepared successfully for operation by the administration over a period of time of large doses of calcium lactate. In some of these cases the hereditary influence could be demonstrated. From time to time, cases of haemophilia calcipriva are found, but the great majority of them have apparently a normal amount of calcium salts. Thus far we have been unable to unravel the mystery.

Purpura is a condition in which the bleeding time is prolonged, and the coagulation time is normal, although the clot does not contract. There is a diminution in the number of blood platelets, and the erythrocytes are easily laked by hypotonic salt solutions. Hess has recently shown that this diminution in blood platelets is only apparent, but not real. There is a diminution in the visible blood platelets and the remaining number are in solution in the plasma. This observer believes that purpura haemorrhagica is caused by some toxin which dissolves blood platelets and injures the blood vessel walls. The poison in some haemolytic diseases is thought to be associated with a disease of the spleen, as the number of blood platelets increases after the spleen has been removed, and it is suggested that splenectomy should be taken into consideration in the course of the treatment of such a disease.

Lee and Robertson have been able to produce experimental purpura in guinea pigs by injecting the serum of a rabbit that had been given immunizing doses of guinea pigs' blood platelets. They found the identical conditions the same as observed in a patient suffering from purpura. We are at present repeating this experiment with the view of producing an anti-platelet serum and if possible applying it to human beings. The purpuras constitute a great variety of cases, differing only in details.

Purpura is not an hereditary disease, although in exceptional instances several cases have been found in one family. In one of our cases now under observation, a child with a normal coagulation time and an intensely prolonged bleeding time, the blood platelets were markedly reduced, and it was found upon further investigation that a similar condition of delayed bleeding time and blood platelet reduction existed in the mother as well as in the father.

In this case there is a probability of the cause being an impairment of the nutrition of the blood vessel wall as the result of the influence of heredity from a syphilitic parent. Calcium administration in this case was of no avail, nor is this remedy expected to be of value in purpuric cases. Unless improvement follows the administration of human serum, this patient will not be operated.

A number of cases have been reported in which the coagulation time and the bleeding time are prolonged and there is a diminution of blood platelets. These cases are very rare, and seem to be a combination of the two diseases.

In anaphylactic conditions the coagulation time is prolonged and very often the bleeding time also prolonged. We have been confronted with this problem in several cases suffering from anaphylaxis due to asthma or pollinosis, where there existed in addition a disease which required operative interference.

R. W., a young woman, with a markedly delayed coagulation time, suffers from asthma due to horse dander. This was successfully treated by immunization methods. In addition there is a complicating ethmoiditis. An unusual degree of secondary oozing for five days took place after the local nasal operation.

It has also been observed that the children of individuals who have an anaphylaxis, who themselves show no symptoms of a disease such as asthma or pollinosis, manifest, however, a decided alteration in the blood coagulability, the same as the parent.

Haemorrhage may be divided, from the therapeutic standpoint, into two classes: continuous, slow, oozing of blood; and active bleeding from a severed or lacerated blood vessel. It should not be a great problem to effectually check the latter variety, even though its site may be difficult of access. The treatment of the former condition depends upon a great many factors. Is the bleeding due to haemophilia, the purpuras, leukemia, anaphylaxis or any other condition in which the coagulation of the blood is prolonged, or is there a disturbance in the nutrition of the lining of the blood vessels, or is there some subtle toxin which produces a destruction of the blood platelets, or destroys the red blood cells, or is there a combination of one or more of these factors?

Therapy, human blood serum, or in its absence of that, diphtheria antitoxin, may be administered either subcutaneously or intravenously. We have given transfusions of whole blood with exceptionally good results in several cases. Of course, in the cases of haemophilia or purpura, the effect of these treatments is only temporary, insofar as it checks only the momentary tendency to bleed or the haemorrhage after operation; it does not cure the primary condition. Many substances have been used which have been found effectual in checking the slow, continuous oozing which has occurred either spontaneously or following operation.

Among these we may mention coagulen, which consists of blood platelets of the horse; thrombokinase, made from the pig's lung,

and thromboplastin, which is macerated brain tissue suspended in saline solution. This last preparation was originated by Hess, and has for its object the counteraction of the antithrombin in the blood; it is efficacious in stopping capillary oozing of moderate severity.

Lowenberg and Rubenstone have recently conducted an experimental research in the effect of glycerinized extracts of visceral tissues on the coagulation time of the blood.

They found that the normal tissue extracts uniformly accelerate the coagulation time of the calcium plasma, and that most of the hemophilic tissues, with the exception of thyroid and liver, seem to exert almost the same influence on coagulation. Thyroid gland and liver not only caused a prolonged coagulation time amounting to two and one-half times the corresponding normal tissues, but actually inhibited the action of the calcium added to the plasma, so that the coagulation of the calcium plasma was prolonged almost two minutes.

These observations were repeated with uniform results, and though admittedly limited to the tissues of one hemophiliac, yet they are strikingly significant, in that there is a possibility that the thyroid and even the liver may secrete an antithrombic substance or enzyme which may be in part, if not principally, the cause of the deranged coagulative mechanism of hemophilic blood.

There are various other biological products which are more or less efficacious, but are too numerous to mention and bear very little relation to the ultimate object of this paper. Calcium salts have been found to be occasionally successful in reducing the coagulation time in those cases in which it is prolonged. When the coagulation time is normal, calcium salts have no effect. This was demonstrated in a series of fifty children having normal coagulation time, who were fed with calcium lactate with no influence.

One of the most difficult conditions to combat is when the bleeding time is prolonged. We have no means at present of absolutely counteracting the substance in the blood which destroys the blood platelets, lessens the resistance of the blood cells or causes a disturbance in the nutrition of the lining of the blood vessel. Occasionally, however, the bleeding time may be shortened by administration of large doses of human serum, as the following cases among a series demonstrates.

A brother and sister were advised to have their tonsils and adenoids removed. In the girl the bleeding and coagulation time was over fifteen minutes, and in the case of the boy, the bleeding time was eight minutes, and the coagulation time fifteen minutes.

Unfortunately at the time, owing to war conditions, we were unable to procure brilliant cresyl blue, which is used in counting blood platelets and this phase of the case was necessarily neglected. The proposition which presented itself was, therefore, one in which the bleeding time and coagulation time were inordinately prolonged, and the other in which the bleeding time was within the range of normal, but the coagulation time was prolonged. Both children were given calcium lactate in large doses over a period of a number of days without appreciable effect. Ten c.c. of the serum obtained from the father's blood was injected intramuscularly into each of the children. One day later the coagulation and bleeding times of the girl were found to be twelve minutes and sixteen minutes, respectively, and in the case of the boy, nine and ten minutes respectively. It was decided to remove the tonsils and adenoids of the boy. He bled considerably during the operation, but not sufficient to be disturbing. Five days after the first serum injection the girl was again given ten c.c. of her father's blood serum. The bleeding and coagulation time two days later was found to be seventeen and nine minutes, respectively. Because the bleeding time still remained prolonged it was decided to defer the operation. Four months later the girl was again tested and her bleeding time was found to be fifteen minutes, and the coagulation time twelve and one-half minutes. Again ten c.c. of her father's blood was injected intramuscularly, and two days later the coagulation time was seven minutes, and the bleeding time six. Tonsillectomy was then performed without any undue bleeding taking place.

In conclusion, let me say that these observations are recorded for the purpose of showing the importance of a little more care in not rushing our patients into operations without sufficient preliminary examinations, and of stimulating further investigation along similar lines hoping to localize the offending principle causing these idiopathic diseases.